PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Masashi OGAWA et al.

Continuation of Appln. No.: 09/125,944 Group Art Unit in Parent: 1631

Confirmation No.: Not Yet Assigned Examiner in Parent: M. MORAN

Filed: July 31, 2001

For: METHOD OF MEASUREMENT OF PROTEASE AND THIN MEMBRANES USED FOR SAID METHOD

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Sir:

Prior to examination, please amend the above-identified application as follows:

IN THE SPECIFICATION:

Please amend the specification by inserting before the first line the sentence:

--This is a continuation of Application No. 09/125,944, filed February 10, 1999, the disclosure of which is incorporated herein by reference.--

IN THE CLAIMS:

Please enter the following amended claims:

1. (amended) A method for measuring protease which comprises the steps of:

(1) contacting a sample containing protease with a thin membrane which comprises a protease substrate together with a hardening agent formed on a surface of a support; and

(2) detecting a trace of digestion formed on the thin membrane by the action of protease.

2. (amended) A method for measuring protease which comprises the steps of:

(1) contacting one of two substantially continuous slices of a biological sample with a thin membrane which comprises a protease substrate together with a hardening agent formed on a surface of a support;

(2) detecting a trace of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion with a histopathological preparation prepared from the other slice.

3. (amended) A method for measuring protease which comprises the steps of:

(1) contacting one of two or more substantially continuous slices of a biological sample with a thin membrane which comprises a protease substrate together with a hardening agent formed on a surface of a support;

(2) contacting the remaining slices with a thin membrane which comprises a protease substrate, a hardening agent, and a protease inhibitor formed on a surface of a support;

(3) detecting traces of digestion formed on the thin membranes by the action of protease; and

(4) comparing the trace of digestion on the thin membrane used in step (1) with the trace of digestion on the thin membrane used in step (2).

4. (amended) A method for measuring protease which comprises the steps of:

(1) contacting one of two or more substantially continuous slices of a biological sample with a thin membrane which comprises a protease substrate together with a hardening agent formed on a surface of a support;

(2) contacting the remaining slices with a thin membrane which comprises a protease substrate different from the protease substrate present in the thin membrane used in step (1) together with a hardening agent formed on a surface of a support;

(3) detecting traces of digestion formed on the thin membranes by the action of protease; and

(4) comparing the trace of digestion on the thin membrane used in step (1) with the trace of digestion on the thin membrane used in step (2).

5. (amended) A method for measuring protease which comprises the steps of:

(1) contacting a sample containing protease with a thin membrane which comprises at least the following two layers: layer (a) which contains a protease substrate, a hardening agent, and a protease inhibitor formed on a surface of a support, and layer (b) which contains a protease substrate and a hardening agent laminated on layer (a);

(2) detecting traces of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion on layer (a) with the trace of digestion on layer (b).

6. (amended) A method for measuring protease which comprises the steps of:

(1) contacting a sample containing protease with a thin membrane which comprises at least the following two layers: layer (a) which contains a protease substrate together with a

hardening agent formed on a surface of a support, and layer (b) which contains a protease substrate different from the protease substrate present in layer (a) together with a hardening agent laminated on layer (a);

(2) detecting traces of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion on layer (a) with the trace of digestion on layer (b).

7. (amended) The method of claim 1 wherein the protease substrate is selected from the group consisting of collagen, gelatin, proteoglycan, fibronectin, laminin, elastin, and casein.

8. (amended) The method of claim 1 wherein the sample is a biological sample isolated or collected from a patient.

9. (amended) The method of claim 1 wherein the detecting by using a thin membrane containing one or more substances selected from the group consisting of metals, metal oxides, pigments and dyes and having a maximum transmission density of 0.01 or higher at a wavelength ranging from 400 nm to 700 nm.

10. (amended) The method of claim 1 wherein the protease is a matrix metalloproteinase.

11. (amended) A thin membrane for measuring protease which contains a protease substrate together with a hardening agent formed on a surface of a support.

12. (amended) The thin membrane of claim 11 which comprises at least the following two layers:

layer (a) which comprises a protease substrate, a hardening agent and a protease inhibitor formed on a surface of a support, and layer (b) which contains a protease substrate together with a hardening agent laminated on layer (a).

13. (amended) The thin membrane of claim 11 which comprises at least the following two layers: layer (a) which comprises a protease substrate together with a hardening agent formed on a surface of a support, and layer (b) which comprises a protease substrate different from the protease substrate present in layer (a) together with a hardening agent laminated on layer (a).

14. (amended) The thin membrane of claim 11 which comprises one or more substances selected from the group consisting of metals, metal oxides, pigments and dyes and have a maximum transmission density of 0.01 or higher at a wavelength ranging from 400 nm to 700 nm.

15. (amended) The thin membrane of claim 11 wherein the support is a microscope slide or a polyethylene terephthalate film.

16. (amended) The thin membrane of claim 11 wherein an undercoat layer is present between the support and the thin membrane.

17. (amended) A method of diagnosing a disease involving protease which comprises the steps of:

(1) contacting a biological sample isolated or collected from a patient with a thin membrane which comprises a protease substrate together with a hardening agent formed on a surface of a support; and

(2) detecting the trace of digestion formed on the thin membrane by the action of protease.

18. (amended) The method of claim 17 wherein the disease is selected from the group consisting of cancer, rheumatic diseases, periodontal diseases and alveolar pyorrhea.

REMARKS

Claims 1-18 have been amended to remove improper multiple dependencies and for editorial purposes only. No new matter has been added.

Entry and consideration of this Amendment is respectfully requested.

Respectfully submitted,

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ a sample containing protease ~~into contact~~ with a thin membrane which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support; and

(2) detecting ~~the~~ a trace of digestion formed on the thin membrane by the action of protease.

2. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ one of two substantially continuous slices of a biological sample ~~into contact~~ with a thin membrane which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support;

(2) detecting ~~the~~ a trace of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion with a histopathological preparation prepared from the other slice.

3. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ one of two or more substantially continuous slices of a biological sample ~~into contact~~ with a thin membrane which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support;

(2) contacting ~~bringing~~ the remaining slices ~~into contact~~ with a thin membrane which comprises a protease substrate, a hardening agent, and a protease inhibitor ~~and is~~ formed on a surface of a support;

(3) detecting traces of digestion formed on the thin membranes by the action of protease; and

(4) comparing the trace of digestion on the thin membrane used in ~~the~~ step (1) with the trace of digestion on the thin membrane used in ~~the~~ step (2).

4. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ one of two or more substantially continuous slices of a biological sample ~~into contact~~ with a thin membrane which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support;

(2) contacting ~~bringing~~ the remaining slices ~~into contact~~ with a thin membrane which comprises a protease substrate different from the protease substrate ~~contained~~ present in the thin membrane used in ~~the~~ step (1) together with a hardening agent ~~and is~~ formed on a surface of a support;

(3) detecting traces of digestion formed on the thin membranes by the action of protease; and

(4) comparing the trace of digestion on the thin membrane used in ~~the~~ step (1) with the trace of digestion on the thin membrane used in ~~the~~ step (2).

5. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ a sample containing protease ~~into contact~~ with a thin membrane which comprises at least the following two layers: layer (a) which contains a protease

substrate, a hardening agent, and a protease inhibitor ~~and is~~ formed on a surface of a support, and layer (b) which contains a protease substrate and a hardening agent ~~and is~~ laminated on ~~the~~ layer (a);

(2) detecting traces of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion on ~~the~~ layer (a) with the trace of digestion on ~~the~~ layer (b).

6. (amended) A method for measuring protease which comprises the steps of:

(1) contacting ~~bringing~~ a sample containing protease ~~into contact~~ with a thin membrane which comprises at least the following two layers: layer (a) which contains a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support, and layer (b) which contains a protease substrate different from the protease substrate present ~~contained~~ in ~~the~~ layer (a) together with a hardening agent ~~and is~~ laminated on ~~the~~ layer (a);

(2) detecting traces of digestion formed on the thin membrane by the action of protease; and

(3) comparing the trace of digestion on ~~the~~ layer (a) with the trace of digestion on ~~the~~ layer (b).

7. (amended) The method of claim 1 ~~any one of claims 1 to 6~~ wherein the protease substrate is selected from the group consisting of collagen, gelatin, proteoglycan, fibronectin, laminin, elastin, and casein.

8. (amended) The method of claim 1 ~~any one of claims 1 to 7~~ wherein the sample is a biological sample isolated or collected from a patient.

9. (amended) The method of claim 1 ~~any one of claims 1 to 8~~ wherein the detecting ~~detection is performed~~ by using a thin membrane containing one or more substances selected from the group consisting of metals, metal oxides, pigments and dyes and having a maximum transmission density of 0.01 or higher at a wavelength ranging from 400 nm to 700 nm.

10. (amended) The method of claim 1 ~~any one of claims 1 to 9~~ wherein the protease is a matrix metalloproteinase.

11. (amended) A thin membrane for measuring protease which contains a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support.

12. (amended) The thin membrane of claim 11 which comprises at least the following two layers:

layer (a) which comprises a protease substrate, a hardening agent and a protease inhibitor ~~and is~~ formed on a surface of a support, and layer (b) which contains a protease substrate together with a hardening agent ~~and is~~ laminated on ~~the~~ layer (a).

13. (amended) The thin membrane of claim 11 which comprises at least the following two layers: layer (a) which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support, and layer (b) which comprises a protease substrate different from the protease substrate ~~contained~~ present in ~~the~~ layer (a) together with a hardening agent ~~and is~~ laminated on ~~the~~ layer (a).

14. (amended) The thin membrane of claim 11 ~~any one of claims 11 to 13~~ which ~~comprise~~ comprises one or more substances selected from the group consisting of metals, metal oxides, pigments and dyes and have a maximum transmission density of 0.01 or higher at a wavelength ranging from 400 nm to 700 nm.

15. (amended) The thin membrane of claim 11 ~~any one of claims 11 to 14~~ wherein the support is ~~selected from~~ a microscope slide ~~and~~ or a polyethylene terephthalate film.

16. (amended) The thin membrane of claim 11 ~~any one of claims 11 to 15~~ wherein an undercoat layer is present ~~provided~~ between the support and the thin membrane.

17. (amended) A method of diagnosing a disease involving protease which comprises the steps of:

(1) contacting ~~bringing~~ a biological sample isolated or collected from a patient ~~into contact~~ with a thin membrane which comprises a protease substrate together with a hardening agent ~~and is~~ formed on a surface of a support; and

(2) detecting the trace of digestion formed on the thin membrane by the action of protease.

18. (amended) The method of claim 17 wherein the disease is selected from the group consisting of cancer, rheumatic diseases, periodontal diseases and alveolar pyorrhea.